REMARKS

Claims 1-10 and 12-30 were pending in the application. Claims 19, 20, and 29 are hereby cancelled without prejudice to pursuing the cancelled claims in this or other continuing applications. Claims 5, 6, 8, 9, 23-25 are withdrawn as being drawn to non-elected subject matter. Claims 1, 3, 8, 9, 12, 14, 16, 18, 24, and 25 have been amended. Upon entry of these amendments, Claims 1-10, 12-18, 23-25, and 30 will be pending and under active consideration. Claims 1, 18, and 25 are independent.

In particular, Claim 1 has been amended to point out more particularly and claim more distinctly that which Applicant regards as his invention by omitting reference to the term wasting disease and incorporating the limitations of canceled Claim 29. Support for the amendment to Claim 1 may be found in original Claim 29 and at page 14, lines 5-6, of the specification as filed and, thus, does not represent new matter. Claim 1 has additionally been amended to omit reference to the terms sepsis and HIV-1. Claim 3 has been amended herein to remove reference to the phrase "or combinations thereof." Claim 3 has additionally been amended herein to more particularly point out and distinctly claim that which applicants regards as his invention by now reciting Met^{358} variants. Applicants submit respectfully that the recitation of Met^{358} variants finds support at page 5, lines 17-30 of the specification as filed and, thus, does not represent new matter. Claim 14 has been amended herein to correct an inadvertent recitation of 200 uM and to recite instead 2000 uM. Applicants submit respectfully that the recitation of "at least .5 μM and no greater than 2000 μM" found in Claim 14, as amended, finds support at page 7, line 24 of the specification as filed and, thus, does not represent new matter.

Applicants wish to thank the Examiner for the withdrawal, noted at paragraph 8 of the Office Action, of the previous objection to Claims 1-17 for having a duplicate member in the Markush group, the withdrawal, noted at paragraph 10 of the Office Action, of the previous rejection of Claims 3, 4, and 22 under 35 U.S.C. § 112, second paragraph, as being allegedly indefinite for the terms α_1-antitrypsin-like agent, variant of α_1-antitrypsin, anticathepsin G agent, antitryptase TL2-agent, antifactor Xa agent, antielastase agent, and antiproteinase-3 agent, and the withdrawal, noted at paragraph 11 of the Office Action, of the previous rejection of Claim 18 under 35 U.S.C. § 112, second paragraph, as being allegedly indefinite for the phrase "exhibiting mammalian α_1-antitrypsin or α_1-antitrypsin-like activity." Applicants also wish to thank the Examiner for the withdrawal, noted at paragraph 14 of the Office Action, of the previous rejection of Claims 4, 9, 12-14, 16, and 24 under 35 U.S.C. § 112, first paragraph, new matter, for the withdrawal, noted at paragraph 15 of the Office Action, of the previous rejection of Claims 1-17 under 35 U.S.C. § 112, first paragraph, enablement, and for the withdrawal, noted at paragraph 16 of the Office Action, of the previous rejection of Claim 18 under 35 U.S.C. § 112, first paragraph, enablement.

Applicant respectfully requests entry of the amendments and remarks made herein into the file history of the present invention. Reconsideration and withdrawal of the rejections set forth in the above-identified Office Action are respectfully requested.

I. The Objection to the Specification at Paragraph No. 7

The Office Action, at paragraph 7, objects to the amendment filed January 29, 2003 (Paper No. 15) is under 35 U.S.C. § 132 because it allegedly introduces new matter into

the disclosure. The Office Action contends that the added material which is not supported by the original disclosure is in non-elected Claim 9 with respect to the limitation of "at least 0.001 and no greater than 7.0 g/kg body weight". Applicant traverses respectfully.

Without acquiescing in the propriety of the rejection, and solely to advance prosecution of the present application, Applicant has amended claim 9, now withdrawn per the Office Action's request, so as to now recite "no greater than 70 g/kg body weight." Support for the amendment to claim 9 is found in the specification as filed at page 7, line 28. Thus, no new matter has been added.

Applicant submits respectfully that the objection to the specification, and in particular, to the amendment to Claim 9 in the prior amendment filed January 29, 2003, under 35 U.S.C. § 132, has been overcome, and Applicant requests respectfully that the 35 U.S.C. § 132 rejection of Claim 9 be withdrawn.

II. The Rejections Under 35 U.S.C. § 102(b) Should Be Withdrawn

The Office Action, at paragraph 22, rejects Claims 1-4 and 30 as allegedly being anticipated by van Molle *et al.*, J. Immunology 159:3556-3564 (1997)(hereinafter, "van Molle"), under 35 U.S.C. § 102(b). The Office Action alleges that van Molle teaches treatment of mice with liver toxicity induced by TNF (tumor necrosis factor) plus GalN (galactosamine) using 0.5 mg of α_1-antitrypsin per mouse. The Office Action further alleges Van Molle monitor the treated mice for apoptosis as measured by the degree of DNA fragmentation in blood samples. Applicant traverses respectfully.

Without acquiescing in the propriety of the rejection, and solely to advance prosecution of the present application, Applicant has amended Claim 1 to no longer recite toxin-induced liver

injury. Applicant submit respectfully that van Molle does not teach, suggest, or motivate the skilled artisan to practice the reduction of apoptosis in mice with any disease condition other than induced liver toxicity, by the use of the serine protease inhibitors or oxidation-resistant or free radical-resistant variant of α_1-antitrypsin, as claimed in Claims 1-4 and 30, as amended.

Applicant submits respectfully that in view of the amendment to Claim 1 to no longer recite the term induced liver oxicity, the rejection of Claims 1-4 and 30 under 35 U.S.C. § 102(b) has been overcome and Applicant requests respectfully that the rejection of Claims 1-4 and 30 under 35 U.S.C. § 102(b) be withdrawn.

The Office Action, at paragraph 23, rejects Claims 1, 3, 4, 10, 15, and 30 as allegedly being anticipated by Emerson *et al.* (USPN 4,829,054) under 35 U.S.C. § 102(b). The Office Action alleges that Emerson *et al.* teach treatment of humans with ARDS for cases of impending sepsis with α_1-antitrypsin. Treatment includes dosing intravenously at 0.1 g/kg (or 100 mg/kg) as demonstrated in the experimental protocol using sheep as a mammalian model. Applicant traverses respectfully.

Without acquiescing in the propriety of the rejection, and solely to advance prosecution of the present application, Applicant has amended Claim 1 to no longer recite sepsis. Applicant submit respectfully that Emerson does not teach, suggest, or motivate the skilled artisan to practice the reduction of apoptosis in humans with any disease condition other than sepsis, by the use of the serine protease inhibitors or oxidation-resistant or free radical-resistant variant of α_1-antitrypsin, as claimed in Claims 1, 3, 4, 10, 15, and 30, as amended.

Applicant submits respectfully that in view of the amendment to Claim 1 to no longer recite the term sepsis, the rejection of Claims 1, 3, 4, 10, 15, and 30 under 35 U.S.C. § 102(b) has

been overcome and Applicant requests respectfully that the rejection of Claims 1, 3, 4, 10, 15, and 30 under 35 U.S.C. § 102(b) be withdrawn.

The Office Action, at paragraph 24, rejects Claims 1, 3, 4, 10, 12-16, and 30 as allegedly being anticipated by Lezdey *et al.* (USPN 5,532,215) under 35 U.S.C. § 102(b). The Office Action alleges that Lezdey *et al.* teach methods of treating viruses in human, particularly HIV infection, with α_1-antitrypsin in daily doses of about 0.06 to 1.2 mg/kg body weight using infusible compositions to maintain a high blood concentration. Applicant traverses respectfully.

Without acquiescing in the propriety of the rejection, and solely to advance prosecution of the present application, Applicant has amended Claim 1 to no longer recite HIV-1. Applicant submit respectfully that Lezdey does not teach, suggest, or motivate the skilled artisan to practice the reduction of apoptosis in humans with any disease condition other than HIV-1, by the use of the serine protease inhibitors or oxidation-resistant or free radical-resistant variant of α_1-antitrypsin, as claimed in Claims 1, 3, 4, 10, 12-16, and 30, as amended.

Applicant submits respectfully that in view of the amendment to Claim 1 to no longer recite the term HIV-1, the rejection of Claims 1, 3, 4, 10, 12-16, and 30 under 35 U.S.C. § 102(b) has been overcome and Applicant requests respectfully that the rejection of Claims 1, 3, 4, 10, 12-16, and 30 under 35 U.S.C. § 102(b) be withdrawn.

The Office Action, at paragraph 25, rejects Claim 18 as allegedly being anticipated by Emerson *et al.* (USPN 4,829,054) as evidenced by Mahidhara *et al.* (Apoptosis and sepsis. Crit. Care Med. (2000) 28:4 (Suppl.)) under 35 U.S.C. § 102(b). The Office Action alleges that Emerson *et al.* teach that "[i]n cases of impending sepsis and shock, prophylactic administration of AT-III and alpha-1-PI should be beneficial"; AT-III is antithrombin III, a serine protease inhibitor, and alpha-l-PI is α_1-proteinase inhibitor (a.k.a. α_1-antitrypsin as per Registry Number

9041-92-3). The Office Action further alleges that sepsis is linked to apoptosis as evidenced by Mahidhara *et al.* Applicant traverses respectfully.

Without acquiescing in the propriety of the rejection, and solely to advance prosecution of the present application, Applicant has canceled Claim 18. Applicant submits respectfully that in view of the cancelation of Claim 18, the rejection of Claim 18 under 35 U.S.C. § 102(b) has been overcome and Applicant requests respectfully that the rejection of Claim 18 under 35 U.S.C. § 102(b) be withdrawn.

The Office Action, at paragraph 26, rejects Claim 19-20 as allegedly as being anticipated under 35 U.S.C. § 102(a) by, or in the alternative, under 35 U.S.C. § 103(a) as obvious over Van Molle *et al.* Van Molle is cited by the Office Action for the reasons of record. The Office Action further alleges that Van Molle teach treatment of mammalian HepG2 cell lines with 0.25 mg/ml α_1-antitrypsin (5 μM). The Office Action alleges that while Van Molle *et al.* report no detected inhibition of apoptosis, this administration of α_1-antitrypsin, at this concentration, is within Applicants' proposed administration range for effect. Applicant traverses respectfully.

Without acquiescing in the propriety of the rejection, and solely to advance prosecution of the present application, Applicant has canceled Claims 19-20. Applicant submits respectfully that in view of the cancelation of Claims 19-20, the rejection of Claims 19-20 under 35 U.S.C. § 102(b) has been overcome and Applicant requests respectfully that the rejection of Claims 19-20 under 35 U.S.C. § 102(b) be withdrawn.

III. Rejecti ns Under 35 U.S.C. § 112, First Paragraph

A. Rejection Of Claim 14 At Paragraph 14 Of The Office Action

At paragraph 18 of the Office Action, Claim 14 is rejected under 35 U.S.C. § 112, first paragraph, new matter, as allegedly failing to comply with the written description requirement. The Office Action contends that Claim 14 contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In particular, the Office Action contends that the limitation of "no greater than 200 μM" is considered new matter. Applicants traverse respectfully.

Without acquiescing in the propriety of rejection, and solely to advance prosecution of the present application, Claim 14 is amended herein to replace the inadvertent recitation of 200 μM with the recitation of 2000 μM. Support for the amendment to Claim 14 may be found in the specification as filed at page 7, line 16.

Applicant submits respectfully that the rejection of Claim 14 under 35 U.S.C. § 112, first paragraph, new matter, has been overcome, and Applicant requests respectfully that the 35 U.S.C. § 112, first paragraph, new matter rejection of Claim 14 be withdrawn.

B. Rejection Of Claims 3-4 At Paragraph 19 Of The Office Action

At paragraph 19 of the Office Action, Claims 3-4 are rejected under 35 U.S.C. § 112, first paragraph, written description, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. The Office Action contends that Claims 3 and 25 utilize, as an option, an oxidation-resistant or free radical-resistant variant of α_1-antitrypsin wherein the use of this serine protease inhibitor is claimed solely by function and without any structural limitations. Applicants traverse respectfully.

Applicant respectfully wishes to draw the attention of the Examiner to the specification at page 5, lines 17-30, and page 17, lines 19-24, wherein specific teaching is provided regarding at least two species of Met^{358} variants that Applicant was in possession of at the time the above-identified application was filed. In particular, the specification provides two examples of Met^{358} variants including Val^{358}-α_1-antitrypsin and Ile^{358}-antitrypsin. Applicant respectfully submits that one of skill in the art may indeed be able to produce additional Met^{358} variants by replacing the Met^{358} amino acid with any hydrophobic or neutral oxidation-resistant amino acid residue as described in the specification as filed at page 5, lines 22-30.

Nevertheless, without acquiescing in the propriety of rejection, and solely to advance prosecution of the present application, Applicant has amended Claim 3 so as to now recite Met^{358} variants. Applicant additionally respectfully wishes to point out to the Examiner that as Claim 25 has been withdrawn, Claim 25 has not been amended at this time.

C. Rejection Of Claims 3-4 At Paragraph 20 Of The Office Action

At paragraph 20 of the Office Action, Claims 3-4 are rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being possibly enabling for methods using known oxidation-resistant or free radical-resistant α_1-antitrypsin variants, allegedly does not reasonably provide enablement for methods using

unknown oxidation-resistant or free radical-resistant α_1-antitrypsin variants. The Offce Action contends that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims and that to practice the claimed methods effectively to the extent they are claimed would allegedly require undue experimentation. Applicant traverses respectfully.

Applicant respectfully submits that, as above for the alleged written description rejection, the specific teaching provided at page 5, lines 17-30, and page 17, lines 19-24 of the specification regarding at least two species of Met^{358} variants that Applicant was in possession of at the time the above-identified application was filed would permit one of skill in the art to practice the claimed invention without undue experimentation. Moreover, Applicant respectfully submits that one of skill in the art would indeed be able to produce additional Met^{358} variants by replacing the Met^{358} amino acid with any hydrophobic or neutral oxidation-resistant amino acid residue as described in the specification as filed at page 5, lines 22-30, and would be able to determine whether or not those additional Met^{358} variants are capable of exhibiting oxidation resistance due to stability of the variant to the neutrophil oxidative burst.

On this basis, Applicant submits respectfully that the rejection of Claims 3-4 under 35 U.S.C. § 112, first paragraph has been overcome, and Applicant requests respectfully that the 35 U.S.C. § 112, first paragraph, rejection of Claims 3-4 be withdrawn.

IV. Rejections Under 35 U.S.C. § 112, Second Paragraph

A. Rejection Of Claims 1-4, 7, 10, 12-20, and 29-30 At Paragraph 12 Of The Office Action

At paragraph 12 of the Office Action, Claims 1-4, 7, 10, 12-20 and 29-30 are rejected under 35 U.S.C. § 112, second paragraph, as being allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the term "wasting disease" is allegedly unclear as to its metes and bounds and that while the specification indicates that the term wasting disease "includes" cancer, neurodegenerative diseases, myocardial infarction, and stroke, the Office Action contends that the term "includes" does not define the metes and bounds of the term "wasting disease". Applicant traverses respectfully.

Without acquiescing in the propriety of rejection, and solely to advance prosecution of the present application, Claim 1 has been amended herein to remove the allegedly indefinite term "wasting disease" and to incorporate the limitations of now canceled Claim 29. Support for the amendment to Claim 1 may be found in canceled Claim 29.

Applicant submits respectfully that the rejection of Claims 1-4, 7, 10, 12-20 and 29-30 under 35 U.S.C. § 112, second paragraph, has been overcome and Applicants request respectfully that the 35 U.S.C. § 112, second paragraph, rejection of Claims 1-4, 7, 10, 12-20 and 29-30 be withdrawn.

B. Rejection Of Claims 1-4, 7, 10, 12-20, and 29-30 At Paragraph 12 Of The Office Action

At paragraph 13 of the Office Action, Claims 3-4 are rejected under 35 U.S.C. § 112, second paragraph, as being allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "and

combinations thereof" allegedly requires clarification as it is whether the combination be an oxidation-resistant variant and a free radical-resistance variant? Applicant traverses respectfully.

Without acquiescing in the propriety of rejection, and solely to advance prosecution of the present application, Claim 3 is amended herein to remove the allegedly indefinite phrase "and combinations thereof".

Applicant submits respectfully that the rejection of Claims 3 and 4 under 35 U.S.C. § 112, second paragraph, has been overcome, and Applicant requests respectfully that the 35 U.S.C. § 112, second paragraph, rejection of Claims 3 and 4 be withdrawn.

CONCLUSION

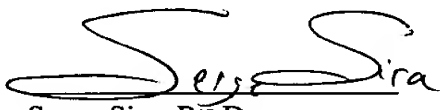
Applicants submit that the application is in condition for allowance. Favorable reconsideration, withdrawal of the rejections set forth in the above-noted Office Action, and an early Notice of Allowance are requested.

Applicants' undersigned attorney may be reached in our Washington, D.C. office by telephone at (202) 625-3500. All correspondence should be directed to our address given below.

AUTHORIZATION

Applicants believe there is no fee due in connection with this filing. However, to the extent required, the Commissioner is hereby authorized to charge any fees due in connection with this filing to Deposit Account 50-1710 or credit any overpayment to same.

Respectfully submitted,



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